

REMARKS

Claims 1-9 are pending in the instant application. Claims 1-4 and 8 and 9 stand rejected as being obvious over the combination of Felder (US 5132409) with either one of Schott DE 29609958 or Walther (US 6200658). Claims 1, 5, 6, 8 and 9 stand rejected as being obvious over Albert (US 5545396) in view of either DE 29609958 or Walther. Claims 1, 5 and 7-9 stand rejected as obvious over the combination of Ardenkjaer-Larsen (US 6466814) with either Schott DE 29609958 or Walther. These rejections are respectfully traversed. Reconsideration is respectfully requested.

1. Claim Rejections : 35 USC §103(a): Claims 1-4, 8 and 9.

Claims 1-4 and 8 and 9 continue to be rejected as obvious over the combination of Felder (US 5132409) with either one of Schott DE 29609958 or Walther (US 6200658). This rejection is respectfully traversed.

Applicants respectfully submit that in upholding this and the other rejections from the previous Office Action, the Examiner has committed several mistakes of interpreting and applying the law as well as in interpreting the science of the cited references.

The present invention is directed to a silica-coated vial containing a specific type of diagnostic agent. "Diagnostic agent" is a term defined in the present application in the first full paragraph of page 4. Claim 1 further restrictively recites that the diagnostic agent claimed is either a non-radioactive metal complex or a hyperpolarized material.

Felder teaches a plurality of macrocyclic chelating agents and chelates thereof. In several examples, Felder discloses that the solution may be diluted and put into vials. Felder neither discloses the material of the vials nor discusses any specifics of the vials whatsoever.

Schott teaches a silica-coated vial for use with pharmaceuticals or diagnostic agents. Schott provides no further description of the contained material other than this generic reference to 'pharmaceuticals' or 'diagnostic agents'.

Walther discloses a glass tube with an oxide coating. Walther notes that the prior art taught a silica-coated tube for use with (generically) pharmaceuticals. Walther contains no reference to diagnostic agents or contrast agents per se.

The Examiner's rejection is premised on the following:

1. Felder discloses contrast agents in vials.
2. The secondary references provide the significance of contrast agents and other pharmaceuticals in vials.
3. Given the disclosure of Felder of contrast agents and pharmaceuticals in vials, one skilled in the art would be motivated to use improved vials.

Applicants will address each of these characterizations below, but note that the Court of Appeals for the Federal Circuit has outlined the requirements for establishing a prima facie case of obviousness.

First, [i]t is impermissible within the framework of 35 U.S.C. §103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation of what such reference fairly suggests to one skilled in the art. *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 796 F.2d 443 (Fed. Cir. 1986). (emphasis added). Something in the prior art as a whole must suggest the desirability, and thus the obviousness, of making the combination. *Uniroyal, Inc. v. Rudkin-Wiley Corp.*, 837 F.2d 1044, 1051 (Fed. Cir. 1988). (emphasis added). It is insufficient that the prior art disclosed the components of the patented device, either separately or used in other combinations; there must be some teaching, suggestion, or incentive to make the combination made by the inventor. *Northern Telecom Inc. v. Datapoint Corp.*, 908 F.2d 931, 934 (Fed. Cir. 1990). (emphasis added).

Applicants respectfully submit that the Examiner has applied Felder not on the basis of Felder as a whole, but by picking out a feature of Felder – the vial - on which Felder does not even elaborate. Applicants have pointed out that the word ‘vial’ is mentioned briefly in Examples 14-19, but the detailed description at Columns 1-8 plus Examples 1-13 and the claims of Felder are all silent on vials. As stated above, Felder is directed to macrocyclic chelating agents and Applicants submit that the focus of Felder, as a whole, is on the preparation of chelating agents, not on a ‘teaching’ that the agents may be put into a vial. Felder provides no description on the details of the vial, indeed there is no suggestion that the vial is critical to the invention, it is simply what the solution is stored in. No fair reading of Felder provides a motivation that the vial should be improved to the benefit of the invention, Felder seems wholly satisfied with the vial as it is. That the Examiner has fixated on the vial of Felder suggests to Applicants that the Examiner is simply picking and choosing from Felder only that which will support his position, not what Felder fairly suggests to one of ordinary skill in the art.

With respect to the secondary references, Applicants note that it has long been the case that “[a] basic mandate inherent in 35 U.S.C. §103 is that “a piecemeal reconstruction of prior art patents in light of the appellants’ disclosure” shall not be the basis for a holding of obviousness.” In re Kamm and Young, 452 F.2d 1052. (C.C.P.A. 1972). Applicants respectfully submit that the Examiner’s reasoning regarding these references evidences an improper piecemeal reconstruction of the present invention.

The Examiner asserts that:

“The secondary references provide the significance of contrast agents and other pharmaceuticals in vials.”

Later, in supporting the rejection, the Examiner states that:

“The secondary references teach that pharmaceuticals, including contrast agents, benefit from being in silica-coated vials”;

The Examiner then relies on a similar characterisation of the prior art at other places in the instant Office Action.

Applicants question the factual basis for these statements. First, only Schott refers to 'diagnostic agents' while Walther refers only to "pharmaceuticals". These are very broad terms, about as generic as they could possibly be to have any relevance to the present invention. Applicants submit that the Examiner is committing clear error in then paraphrasing these documents as specifically relating to 'contrast agents'. Neither reference uses the term 'contrast agents', let alone the term 'diagnostic agent' as that is restrictively defined or claimed by the present invention, yet the Examiner continuously asserts that these references disclose contrast agents. Applicants respectfully submit that by making such a leap from what the prior art actually states to what the Examiner characterizes the references as stating is an indication of the Examiner's improper use of the Applicants own disclosure as a blueprint for reconstructing the present invention in piecemeal fashion.

Then, in ascribing a motivation provided by the art to combine the references in accordance with the rejection, the Examiner states that all of the teachings in the art would be considered and "given the disclosure of Felder of contrast agents and pharmaceuticals in vials, one skilled in the art would be motivated to use improved vials." Applicants respectfully submit that such a statement is both logically and legally unsupportable.

The Examiner's assertion is logically unsupportable because Felder provides no discussion of a vial other than to note one is used to hold the diluted solution. Felder makes no mention of the vial's construction, material or the like. Applicants submit that a more reasonable conclusion is that Felder's silence with respect to the vial is that Felder is altogether happy with the vial and saw no need to further improve it.

Likewise, the Examiner's assertion that given Felder's disclosure of a vial that one would be motivated to use improved vials flies in the face of Federal Circuit precedent. Indeed the Examiner's reasoning vitiates the Federal Circuit prohibition of 'selective picking

and choosing' since it rests on the mere fact that something was disclosed in the reference regardless of the requirement of having to reflect on what the reference as a whole suggests to one of ordinary skill per Uniroyal.

Thus, Applicants respectfully submit that by focusing on an extremely minor aspect of Felder, by mischaracterizing the teachings of Schott and Walther, and by failing to properly demonstrate a motivation for combining these particular features of each reference, the Examiner has failed to establish a prima facie case of obviousness against the present invention.

Moreover, the Examiner has rejected Applicants arguments of how Felder teaches away from the present invention. In making his 'teaching away' arguments, Applicants note that the Examiner is incorrect as a matter of law. The Examiner states that "One improvement is not a teaching away from other" [sic]. The Examiner also states that "There is nothing to suggest that one skilled in the art would limit themselves to the specific benefits taught by Felder". Later, the Examiner states that "a teaching away is provided when the art actually teaching a negative aspect is obtained by a certain modification". Applicants submit that none of these citations are correct – 'teaching away' simply means teaching a solution that would not lead to the claimed subject matter. The Federal Circuit has spoken to this very point:

A reference may be said to teach away when a person of ordinary skill, upon [examining] the reference would be discouraged from following the path set out in the reference, or would be led in a direction divergent from the path that was taken by the applicant. (emphasis added).

Para-Ordnance Mfg. v. SGS Importers Int'l, 73 F.3d 1085 (Fed. Cir. 1995).

Therefore, Applicants submit that, contrary to the Examiner's assertions, one improvement can teach away from another, the two improvements may diverge from each other in their teachings. Also, it is incorrect to conclude that "[t]here is nothing to suggest that one skilled in the art would limit themselves to the specific benefits taught by Felder" because such a conclusion requires a negative teaching in order to find a teaching away while it also ignores the requirement to consider what the reference suggests as a whole. Lastly,

the Para-Ordinance decision clearly states that teaching away does not require a negative teaching in the prior art, the prior art need only teach other, divergent, solutions to be found to teach away from an invention.

Thus, by teaching positively towards certain embodiments or features as being important or preferred, the art provides a motivation for the person skilled in the art to go in a particular direction. If that direction leads towards subject matter outside the scope of the claims at issue, then it constitutes a "teaching away". Applicants maintain that the person skilled in the art, even if assumed to be contemplating an improvement of Felder, would focus on the teachings in Felder of embodiments taught to be important, and be motivated to improve those elements. In Felder these are clearly the design of the chelating agent, which is described at length at Column 5 line 25 to Column 7 line 65. That constitutes four columns of text. Again, Felder itself does not even discuss vials or containers, and hence gives no weight to that feature. Felder's emphasis on the chelating agents, and apparent satisfaction with the featureless vial would indicate that improvements to the solution are found by adjusting the formulation of the solution, not by modifying the featureless container.

The Examiner also dismisses the Applicants suggestion that the Examiner has employed improper hindsight by invoking the language of *In re McLaughlin*. Applicants respectfully submit, however, that the Examiner's rejection does take into account knowledge found in the present application.

The Examiner contends that since silica-coated vials are known to have 'benefits' for pharmaceuticals, one of skill in the art would be motivated to combine such vials with the contrast agents of Felder. If the Examiner is going to treat the present invention as a combination invention, Applicants note that the Federal Circuit has directed for combination inventions that:

The initial inquiry should be directed to the vantage point of attacking the problem solved by the invention at the time the invention was made. When prior art itself does not suggest or render 'obvious' the claimed solution to that

problem, the art involved does not satisfy the criteria of 35 U.S.C. §103 for precluding patentability.
Lindemann Maschinenfabrik GmbH v. American Hoist and Derrick Co., 730 F.2d 1452 (Fed. Cir. 1984).

Applicants have stressed that the present invention describes at length how diagnostic agent metal complexes suffer from unforeseen or variable problems which are solved using silica-coated vials. See page 5 line 1 to page 7 line 22 of the present specification. These problems were not recognised in the prior art, and hence the cited references do not suggest applying silica-coated vials to diagnostic agent metal complexes. The solution to the problem provided by the present claims is therefore believed non-obvious over the cited references.

Further comments on the specific document combinations cited by the Examiner are given below:

1.1 Felder and DE 29609958.

The Examiner argues that:

“The leaching problem is taught in the art, by DE ‘958, that various pharmaceuticals and diagnostic agents suffer from leaching and that problem can be prevented by using silica coated vials. Clearly, one skilled in the art would see that the benefit would hold true for various pharmaceuticals and diagnostic agents, as taught by DE ‘958, such as the pharmaceutical/diagnostic agents disclosed by Felder.”

The Examiner seemingly accepts the fact that Felder itself does not teach or suggest that the diagnostic agent metal complexes described therein suffer from any of the leaching problems. Applicants contend that the Examiner’s phrase ‘various pharmaceuticals and diagnostic agents’ is general only, and fails to demonstrate specific motivation to combine with Felder. The phrase “such as...disclosed by Felder” confirms that Felder is merely illustrative of *any* diagnostic agent. Such logic

merely reiterates the teaching of DE '958. It does not show why the specific combination with Felder would definitely have been made. Consequently, the objection also shows that the purported motivation originates from "benefits" within the vial prior art in isolation, not from the required 'obviousness' combination ie. [DE '958] + [Felder].

DE '958 teaches that glass containers having an inner surface coating of oxides or nitrides of silicon, titanium, tantalum and/or aluminium are useful to reduce leaching of impurities from the glass walls into the contents. There is no teaching or suggestion in Felder that the compositions therein suffer from such leaching problems. Hence, applicants contend that there would be no motivation for the person skilled in the art to modify Felder in the manner suggested by the Examiner.

As noted above, DE '958 teaches that a very wide range of oxide or nitride coating materials can be used. Hence, the combination of [Felder] + [DE '958] leads to a wide range of possibilities, and the person skilled in the art would not be limited to what DE '958 teaches to be important. Consequently, the combination [Felder] + [DE '958] does not lead to the specific teaching of the present claims.

Contrary to the Examiner's characterisation of DE '958 as teaching contrast agents (*see above*), DE '958 teaches only blood and blood samples as examples of the "diagnostic solution." Applicants therefore contend that the person skilled in the art would be unlikely to use DE '958 as a source of teaching applicable to metal complex diagnostic agents which are very different to biological fluids such as blood. Applicants therefore contend that the Examiner's obviousness objection based on this combination of references should be withdrawn. Reconsideration is respectfully requested.

1.2 Felder and Walther.

The Examiner asserts that Walther teaches "only three possibilities" and later

characterizes this as a 'very limited number of possibilities'. Applicants cannot agree that this is an accurate representation of the teachings of Walther. The Examiner's attention is drawn to Claim 1 of Walther (Column 8 lines 2 to 13), where the phrase "oxide material" is used. Walther uses this same phrase at Column 3 lines 23-39 and Column 4 lines 19-34. Neither the claims nor the specification of Walther limit the "oxide material".

Hence, Applicants contend that Walther in fact teaches that a wide range of oxides are to be used, and that the person skilled in the art would not limit their thinking to what is said to be preferred. Hence, the combination [Felder] + [Walther] leads to a wide range of possibilities, not the specific teachings of the present claims.

Walther does suggest (at Column 4 lines 40 to 43) that SiO_2 , Al_2O_3 , TiO_2 or mixtures thereof may be used as a preferred embodiment. Even on that teaching, when "mixtures thereof" are permitted, this does not reduce to three possibilities but the following:

SiO_2 alone;

Al_2O_3 alone;

TiO_2 alone;

SiO_2 plus Al_2O_3 ;

SiO_2 plus TiO_2 ;

Al_2O_3 plus TiO_2 ;

SiO_2 plus Al_2O_3 plus TiO_2 .

That makes a minimum of seven possible combinations, not three, and for those where there are mixtures there is an infinite range of percentage compositions. Hence, the Examiner's characterisation of the teaching of Walther as a choice of three is deeply misleading, and not an accurate reflection of what the reference as a whole suggests or the real choices facing the person skilled in the art upon considering it.

Applicants therefore contend that the obviousness objection based on this

combination should be withdrawn. Reconsideration is respectfully requested.

The Examiner's comments with respect to PCVD (Claim 8) are believed moot, since Claim 8 depends on Claim 1, and the above demonstrates that Claim 1 is non-obvious over the prior art of record. Reconsideration and withdrawal of the rejection are respectfully requested.

Claim Rejections: 35 USC §103(a): Claims 1, 5, 6, 8 and 9.

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The Examiner contends that Claims 1, 5, 6, 8 and 9 are obvious over Albert (US 5545396) in view of either DE 29609958 or Walther. This rejection is respectfully traversed.

Albert discloses the use of hyperpolarized noble gases for MR imaging. Albert further discloses that the hyperpolarized gas may be stored in a container having a silicone coating.

The Examiner again suggests that it would be obvious to combine the teaching of either DE '958 or Walther on silica-coated vials with the hyperpolarized gas of Albert. The Examiner contends that since silica-coated vials are known to have 'benefits' for pharmaceuticals, one of skill in the art would be motivated to combine such vials with the hyperpolarized gas of Albert. The Examiner's contention seems to be, that if a coating is beneficial to some pharmaceuticals, then it must be beneficial to all pharmaceuticals, without regard to how that coating reacts with the particular pharmaceutical, or in this case, a hyperpolarized gas. These references include using metals within their coatings which are taught herein to adversely affect the polarization levels of a stored hyperpolarized gas. As there is no disclosure, teaching, or suggestion in any of these references to employ only a silica coating so as to not adversely affect the polarization level of a hyperpolarized noble

gas, the only motivation for so combining these references is provided by the Applicants' own disclosure.

The Examiner states that "one of ordinary skill in the art would have been motivated to use such silica coated vials for the pharmaceutical compositions disclosed by Albert to take advantage of the one or all of the advantages taught in the prior art in using such vials for pharmaceuticals." Applicants submit that this is another example of the Examiner inventing a justification for combining the prior art so as to read on the present invention without regard to what these references as a whole would fairly suggest to one of ordinary skill in the art. Albert teaches that silicone should be employed for storing a hyperpolarized gas. One of skill in the art looking at these references would be motivated to follow Albert's specific teachings for preserving the polarization of Albert's own disclosed contrast agent, not the teachings of either Schott or Walther. The Examiner has provided no basis for disposing of Albert's coating in favour of one of the coatings of the secondary references. Once again, the Examiner has used the Applicants' own disclosure as a blueprint for forming an obviousness argument. Since the cited references provide no disclosure, teaching, or suggestion for selecting one of the coatings of the secondary references over the specific coating of the primary reference for use with a hyperpolarized gas, the present invention is patentably distinct thereover. Reconsideration and withdrawal of the rejection are respectfully requested.

Furthermore, the Examiner states in this Office Action that Applicants had previously asserted that "Albert teaches silicon to solve a problem, which is different from silica" and then proceeds to argue against this reasoning and questions Applicants' references to 'silicon'.

Unfortunately, the Examiner has completely misread Applicants' previous response. That response clearly referred to Albert's teachings with respect to silicone which is *very* different from silicon. Silicone is indeed a "synthetic polymer containing a repeating silicon oxygen backbone with organic side groups attached *via* carbon-silicon bonds (Merck Index,

13th Edition, entry no. 8569). Consequently Applicants arguments were not “somewhat vague”, but factually correct. The Examiner is invited to study the response as filed and withdraw this wholly inaccurate characterisation of the response.

Applicants repeat that Albert at Example 2 (Column 19 lines 1 to 55, especially lines 8-10) specifically teaches that a silicone coating is to be used and is effective to reduce relaxation of the hyperpolarised ^{129}Xe gas on the walls of the glass vessel. The present claims specify silica, ie. SiO_2 which is not carbon-containing. Silicon, silica and silicone are very different chemical species, but unfortunately the Examiner seems to be confusing them. These, and the statements made in Albert are matters of fact, which the Examiner is invited to confirm.

Applicants note that their previous quotation from Example 2 of Albert is regarded as “out of context”, but cannot agree with this characterisation. Example 2 of Albert refers to silicone coating of glass vessels/containers for the hyperpolarised ^{129}Xe gas, and at Column 19 Lines 13-14 to flame sealing. Flame sealing a gas in a glass vessel is standard practice for the storage of gases, and for the Examiner to suggest otherwise is factually incorrect. Thus, Example 2 is entirely consistent with Example 3, and indeed the rest of Albert.

Applicants refer to the statement at Column 19 lines 8 to 10 of Albert:

“The silicone coating apparently reduces relaxation of ^{129}Xe on the walls of the glass sphere, permitting creation of larger polarisations.”

Thus, Albert provides clear teaching of how to solve the problem of storage of the hyperpolarised gas in glass vessels, by using a silicone coating. The Examiner’s combination of references therefore contradicts Albert itself, and provides no basis for choosing the coatings of Schott or Walther over the coatings of Albert. Reconsideration and withdrawal of the rejection are respectfully requested.

3. Claim Rejections: 35 USC §103(a): Claims 1, 5 and 7-9.

Claims 1, 5 and 7-9 are rejected as obvious over the combination of Ardenkjaer-Larsen (US 6466814) with either Schott DE 29609958 or Walther. This rejection is respectfully traversed.

Ardenkjaer-Larsen discloses the use of ^{13}C -labelled hyperpolarised compounds for imaging.

As has been argued at length above, DE '958 teaches a wide range of vial coating material possibilities. The combination [Ardenkjaer-Larsen] + [DE '958] therefore leads to a wide range of possibilities, which the Examiner has stated the person skilled in the art would consider in full. The combination therefore does not lead directly to the specific subject matter of the present claims. Consequently, the present claims are believed non-obvious over the combination.

Furthermore, as noted above, DE '958 teaches only blood and blood products as possible diagnostic agents which could benefit from being used in such coated vials. Hence, the person skilled in the art is unlikely to regard such vials as being useful for very different agents such as ^{13}C -labelled hyperpolarised materials.

Similar logic applies to Walther, which also teaches a wide range of possibilities, as discussed above. The combination therefore does not lead directly to the specific subject matter of the present claims. Consequently, the present claims are believed non-obvious over the combination. Reconsideration and withdrawal of the rejection are respectfully requested.

In view of the remarks hereinabove, Applicants respectfully submit that the present invention, including claims 1-9, is patentably distinct over the prior art. Favorable action thereon is respectfully requested.

Appl. No. 10/069,690
Amdt. Dated January 10, 2005
Reply to Office action of November 9, 2004

Applicants note that this response is being filed within two months of the mailing date of this final action.

Any questions with respect to the foregoing may be directed to Applicants' undersigned counsel.

Respectfully submitted,

A handwritten signature in black ink, appearing to read 'R. Chisholm', written over a horizontal line.

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